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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,237	10/19/2000	David S. Wells	085747/0170	5026

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EXAMINER	
CHANNAVAJJALA, LAKSHMI SARADA	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/691,237	WELLS ET AL.	
	Examiner	Art Unit	
	Lakshmi S. Channavajjala	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35,37-42,44-55 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,37-42,44-55 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

JLC

DETAILED ACTION

Receipt of amendment and remarks dated 12-9-04 is acknowledged.

Claims 35, 37-42, 44-55 and 57 are pending in the instant application.

The following rejection of record has been maintained:

Claim Rejections - 35 USC § 103

Claims 35, 37-39, 41, 42, 47, 51-54 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/44623 (WO) in view of Hsiao US 4,571,333 (Hsiao).

Please note that the rejection of claims as being obvious over Hsiao in view of WO has been withdrawn and only WO in view of Hsiao has been maintained.

Hsiao teaches sustained release formulations comprising naproxen and naproxen salts in the form of oral tablets suitable for once-daily administration. The naproxen composition of Hsiao is made of a matrix composition 81-96% % by weight of naproxen and 4-9% by weight of hydroxypropyl methylcellulose and other excipients (examples, col. 4, lines 59-68 and col. 5, lines 1-4). Hsiao does not teach the claimed active agents.

WO teaches compositions comprising valerian extracts, isovaleric acid and their derivatives in combination with non-steroidal anti-inflammatory compounds such as naproxen, ibuprofen etc (page 14-page 17). Isovaleric acid and other valerian extracts taught by WO read on the instant claimed active agents. WO further teaches that the oral isovaleramide or valerian extract containing compositions, together with anti-inflammatory compounds can be prepared in the form of enteric-coated tablets, capsules etc., so as to successfully treat muscular aches, pain, as well as inflammation.

WO fails to teach a gelling agent or matrix formulation for the above active agents. However, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to prepare the composition of WO containing isovaleramide, isovaleric acid or valerian extracts and anti-inflammatory agents such as naproxen in the form of an oral sustained release matrix by adding a sustained release swelling agent, HPMC, because Hsiao teaches that the pain or inflammation treating composition prepared in a matrix with HPMC prolongs the release of the active agent so as to achieve a once-a-day administration. Alternatively, it would have been obvious for a skilled artisan at the time of the instant invention to add valerian extracts, isovaleramide etc. to the anti-inflammatory naproxen containing composition of Hsiao because WO suggests that the combination treats inflammation as well as provides a relief from acute pain and muscular tension. With respect to the claimed weight percentage, WO teaches upto 600 mg of active ingredient per tablet and further, the percentages of active ingredient and HPMC taught by Hsiao are within the claimed ranges. With respect to the process of preparing the composition, Hsiao teaches the same steps of mixing the ingredients, extruding and compressing to form tablets (col. 7). Accordingly, optimizing the amount of drug and the release agent, as well as choosing an appropriate release agent so as to achieve the desired release rate are within the scope of a skilled artisan.

Claims 40, 44-46, 48-50, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,571,333 to Hsiao in view of WO 99/44623 or WO in view of

Hsiao as applied to claims 35, 37-39, 41, 47, 51-54 and 57 and further in view of Groshovy et al (Groshovy, submitted on PTO-1449).

Hsiao and WO, discussed above, fail to teach a film coating that retards the access of the liquids to the active compounds.

Groshovy teaches coating of tablets with intestine soluble film forming polymer such as acetylphthalylcellulose so as to enhance the physical strength and resistance to the action of gastric juice (page 1). Groshovy teaches tablets containing valerian extracts are usually destroyed by gastric juices in two hours and the resulting weight loss prompts the addition of plasticizers to the film-forming substances (page 4). Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ a film-forming coat over the oral composition of WO containing valerian extracts and anti-inflammatory such as naproxen in the form of a sustained release matrix containing HPMC (the sustained release agent of Hsiao) because Groshovy teaches that tablets containing valerian extracts are sensitive to gastric juices and a film-forming polymer together with a plasticizer reduces the sensitivity of the composition to gastric juices and the plasticizer enhances the strength of the film surrounding the composition.

Response to Arguments

Applicant's arguments filed 12-9-04 have been fully considered but they are not persuasive.

Applicants argue that it was applicants who first recognized that the claimed isovaleramide, isovaleric acid, and the other related compounds have a short half-life in vivo as set forth in example (pages 2 and 5 of the specification) and there was no motivation in the prior art to provide the recited compounds in a sustained-release composition.

Applicants agree that Hsiao (USPN 4,571,333) is directed to sustained-release formulations of naproxen, an NSAID. Artman (WO 99/44623) is directed to combination therapies comprising the administration of isovaleramide (or related compounds) and an NSAID. However, they argue that this combination of references does not establish a prima facie case of obviousness of the instant claims, even though Hsiao shows a sustained-release formulation of another drug. It is argued Hsiao teaches away from modification of its invention because the objective of Hsiao is to provide a maximum amount of naproxen (500-1200 mg) in a tablet with minimum bulk and to achieve this goal, the tablets of Hsiao must contain from 81-96% by weight naproxen. This simply does not leave room for a therapeutically effective amount of the active compounds of the present invention. Applicants also argue that 40-70% w/w amount of active compound recited in the claims left no question that compositions based on Hsiao are excluded from the claims, because a composition cannot comprise both 81-96% naproxen and 40-70% w/w isovaleramide compound and that it would be impossible to formulate a composition that comprises both 81-96% naproxen, as required by Hsiao, and 40-70% of the presently claimed active compounds.

Applicants' arguments have been considered but not found persuasive because while it is true that Hsiao teaches a large amount of naproxen, which would not allow any room to add the claimed active compounds, instant rejection is made over WO in view of Hsiao. WO teaches (as admitted by applicants) the claimed compositions and also suggests combinations of isovaleramide and naproxen. The combination of references is to show that it would have been obvious for one of an ordinary skill in the art to add motivation to add HPMC of Hsiao to the composition of WO containing isovaleramide as well as naproxen because Hsiao teaches that the composition prepared in a matrix with HPMC prolongs the release of the active agent so as to achieve a once-a-day administration. With respect to the high amount of naproxen taught by Hsiao, the motivation is to add the HPMC of Hsiao and not naproxen of Hsiao. Further, WO teaches combination of drugs for the same purposes i.e., treating pain and therefore, optimizing the amounts of individual active agents, drawn to treat the same conditions so at to achieve an additive, if not a synergistic effect, depending on if one of an ordinary skill in the art chooses to use isovaleramide alone or isovaleramide in combination with naproxen. With respect to providing sustained release compositions, Hsiao teaches sustained release compositions containing pain treating drugs and that HPMC enables a prolonged release of the drug, thus providing the required motivation for a skilled artisan to prepare pain treating isovaleramide compositions in a sustained release form. Hence, for the above reasons the rejection has been maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is 571-272-0591. The examiner can normally be reached on 9.00 AM -6.30 PM

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lakshmi S Channavajjala
Examiner
Art Unit 1615
March 23, 2005

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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